

WHAT IS CLAIMED

1. An isolated nucleic acid molecule comprising
5 a nucleotide sequence selected from the group
consisting of:

(a) the nucleotide sequence set forth in SEQ ID
NO: 2;

(b) a nucleotide sequence encoding the
10 polypeptide set forth in SEQ ID NO: 1;

(c) a nucleotide sequence which hybridizes under
moderately or highly stringent conditions to the
complement of (a) or (b), wherein the encoded
polypeptide has an activity of the polypeptide set
15 forth in SEQ ID NO: 3 or homodimer or heterodimer
thereof; and

(d) a nucleotide sequence complementary to any of
(a)-(c).

20 2. An isolated nucleic acid molecule comprising
a nucleotide sequence selected from the group
consisting of:

(a) a nucleotide sequence encoding a polypeptide
that is at least about 70, 75, 80, 85, 90, 95, 96, 97,
25 98, or 99 percent identical to the polypeptide set
forth in SEQ ID NO: 1, wherein the polypeptide has an
activity of the polypeptide set forth in SEQ ID NO: 3
or homodimer or heterodimer thereof;

(b) a nucleotide sequence encoding an allelic
30 variant or splice variant of the nucleotide sequence
set forth in SEQ ID NO: 2, wherein the encoded
polypeptide has an activity of the polypeptide set
forth in SEQ ID NO: 3 or homodimer or heterodimer

thereof;

(c) a nucleotide sequence of SEQ ID NO: 2, (a),
or (b) encoding a polypeptide fragment of at least
about 25 amino acid residues, wherein the polypeptide
5 has an activity of the polypeptide set forth in SEQ ID
NO: 3 or homodimer or heterodimer thereof;

(d) a nucleotide sequence of SEQ ID NO: 2 or (a)-
(c) comprising a fragment of at least about 16
nucleotides;

10 (e) a nucleotide sequence which hybridizes under
moderately or highly stringent conditions to the
complement of any of (a)-(d), wherein the polypeptide
has an activity of the polypeptide set forth in SEQ ID
NO: 3 or homodimer or heterodimer thereof; and

15 (f) a nucleotide sequence complementary to any of
(a)-(c).

3. An isolated nucleic acid molecule comprising
a nucleotide sequence selected from the group
20 consisting of:

(a) a nucleotide sequence encoding a polypeptide
as set forth in SEQ ID NO: 1 with at least one
conservative amino acid substitution, wherein the
polypeptide has an activity of the polypeptide set
25 forth in SEQ ID NO: 3 or homodimer or heterodimer
thereof;

(b) a nucleotide sequence encoding a polypeptide
as set forth in SEQ ID NO: 1 with at least one amino
acid insertion, wherein the polypeptide has an activity
30 of the polypeptide set forth in SEQ ID NO: 3 or
homodimer or heterodimer thereof;

(c) a nucleotide sequence encoding a polypeptide
as set forth in SEQ ID NO: 1 with at least one amino

acid deletion, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 3 or homodimer or heterodimer thereof;

(d) a nucleotide sequence encoding a polypeptide
5 as set forth in SEQ ID NO: 1 which has a C- and/or N-terminal truncation, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 3 or homodimer or heterodimer thereof;

(e) a nucleotide sequence encoding a polypeptide
10 as set forth in SEQ ID NO: 1 with at least one modification selected from the group consisting of amino acid substitutions, amino acid insertions, amino acid deletions, C-terminal truncation, and N-terminal truncation, wherein the polypeptide has an activity of
15 the polypeptide set forth in SEQ ID NO: 3 or homodimer or heterodimer thereof;

(f) a nucleotide sequence of (a)-(e) comprising a fragment of at least about 16 nucleotides;

(g) a nucleotide sequence which hybridizes under,
20 moderately or highly stringent conditions to the complement of any of (a)-(f), wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 3 or homodimer or heterodimer thereof; and

(h) a nucleotide sequence complementary to any of
25 (a)-(e).

4. A vector comprising the nucleic acid molecule of Claims 1, 2, or 3.

30 5. A host cell comprising the vector of Claim 4.

6. The host cell of Claim 5 that is a eukaryotic cell.

7. The host cell of Claim 5 that is a prokaryotic cell.

8. A process of producing a β 10 polypeptide or β 10 homodimer comprising culturing the host cell of Claim 5 under suitable conditions to express the polypeptide or homodimer, and optionally isolating the polypeptide or homodimer from the culture.

9. A polypeptide or homodimer produced by the process of Claim 8.

10. The process of Claim 8, wherein the nucleic acid molecule comprises promoter DNA other than the promoter DNA for the native β 10 polypeptide operatively linked to the DNA encoding the β 10 polypeptide.

11. The isolated nucleic acid molecule according to Claim 2 wherein the percent identity is determined using a computer program selected from the group consisting of GAP, BLASTP, BLASTN, FASTA, BLASTA, BLASTX, BestFit, and the Smith-Waterman algorithm.

12. A process for determining whether a compound modulates β 10 polypeptide or β 10 homodimer activity or production comprising exposing a cell comprising the vector of claim 4 to the compound, and measuring β 10 polypeptide or β 10 homodimer activity or production in said cell.

13. An isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 3.

14. An isolated polypeptide comprising the amino

acid sequence selected from the group consisting of:

(a) the mature amino acid sequence as set forth in SEQ ID NO: 3, comprising a mature amino terminus at residue 1, optionally further comprising an amino-terminal methionine;

(b) an amino acid sequence for an ortholog of SEQ ID NO: 3, wherein the encoded polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 3 or homodimer or heterodimer thereof;

(c) an amino acid sequence that is at least about 70, 75, 80, 85, 90, 95, 96, 97, 98, or 99 percent identical to the amino acid sequence of SEQ ID NO: 3, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 3 or homodimer or heterodimer thereof;

(d) a fragment of the amino acid sequence set forth in SEQ ID NO: 3 comprising at least about 25 amino acid residues, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 3 or homodimer or heterodimer thereof;

(e) an amino acid sequence for an allelic variant or splice variant of either the amino acid sequence set forth in SEQ ID NO: 3 or at least one of (a)-(c) wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 3 or homodimer or heterodimer thereof.

15. An isolated polypeptide comprising the amino acid sequence selected from the group consisting of:

(a) the amino acid sequence set forth in SEQ ID NO: 3 with at least one conservative amino acid substitution, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 3 or homodimer or heterodimer thereof;

(b) the amino acid sequence set forth in SEQ ID NO: 3 with at least one amino acid insertion, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 3 or homodimer or heterodimer thereof;

(c) the amino acid sequence set forth in SEQ ID NO: 3 with at least one amino acid deletion, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 3 or homodimer or heterodimer thereof;

(d) the amino acid sequence set forth in SEQ ID NO: 3 which has a C- and/or N-terminal truncation, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 3 or homodimer or heterodimer thereof; and

(e) the amino acid sequence set forth in SEQ ID NO: 3, with at least one modification selected from the group consisting of amino acid substitutions, amino acid insertions, amino acid deletions, C-terminal truncation, and N-terminal truncation, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 3 or homodimer or heterodimer thereof.

16. An isolated polypeptide encoded by the nucleic acid molecule of Claims 1, 2, or 3.

17. The isolated polypeptide according to Claim 14 wherein the percent identity is determined using a computer program selected from the group consisting of GAP, BLASTP, BLASTN, FASTA, BLASTA, BLASTX, BestFit, and the Smith-Waterman algorithm.

18. An antibody produced by immunizing an animal with a peptide comprising the amino acid sequence of

SEQ ID NO: 3.

19. An antibody or fragment thereof that specifically binds the polypeptide of Claims 13, 14, or
5 15.

20. The antibody of Claim 19 that is a monoclonal antibody.

10 21. A hybridoma that produces a monoclonal antibody that binds to a peptide comprising the amino acid sequence of SEQ ID NO: 3.

22. A method of detecting or quantitating the
15 amount of β 10 polypeptide using an anti- β 10 antibody or fragment thereof which specifically binds the polypeptide of claims 13, 14 or 15.

23. A selective binding agent or fragment thereof
20 that specifically binds at least one polypeptide, wherein said polypeptide comprises the amino acid sequence selected from the group consisting of:

a) the amino acid sequence set forth in SEQ ID NO:
25 3; and

b) a fragment of the amino acid sequence set forth in SEQ ID NO: 3; and

c) a naturally occurring variant of (a) or (b).

24. The selective binding agent of Claim 23 that
30 is an antibody or fragment thereof.

25. The selective binding agent of Claim 23 that
is a humanized antibody.

35

26. The selective binding agent of Claim 23 that is a human antibody or fragment thereof.

27. The selective binding agent of Claim 23 that is a polyclonal antibody or fragment thereof.

28. The selective binding agent of Claim 23 that is a monoclonal antibody or fragment thereof.

29. The selective binding agent of Claim 23 that is a chimeric antibody or fragment thereof.

30. The selective binding agent of Claim 23 that is a CDR-grafted antibody or fragment thereof.

31. The selective binding agent of Claim 23 that is an anti-idiotypic antibody or fragment thereof.

32. The selective binding agent of Claim 23 which is a variable region fragment.

33. The variable region fragment of Claim 32 which is a Fab or a Fab' fragment.

34. A selective binding agent or fragment thereof comprising at least one complementarity determining region with specificity for a polypeptide having the amino acid sequence of SEQ ID NO: 3.

35. The selective binding agent of Claim 23 which is bound to a detectable label.

36. The selective binding agent of Claim 23 which antagonizes β 10 polypeptide biological activity.

37. A method for treating, preventing, or ameliorating a disease, condition, or disorder comprising administering to a patient an effective amount of a selective binding agent according to
5 Claim 23.

38. A selective binding agent produced by immunizing an animal with a polypeptide comprising the amino acid sequence of SEQ ID NO: 3.
10

39. A hybridoma that produces a selective binding agent capable of binding a polypeptide according to Claims 1, 2, or 3.

40. A composition comprising the polypeptide of Claims 13, 14, or 15 and a pharmaceutically acceptable formulation agent.
15

41. The composition of Claim 40 wherein the
20 pharmaceutically acceptable formulation agent is a carrier, adjuvant, solubilizer, stabilizer, or anti-oxidant.

42. The composition of Claim 40 wherein the
25 polypeptide comprises the mature amino acid sequence as set forth in SEQ ID NO: 3.

43. A polypeptide comprising a derivative of the polypeptide of Claims 13, 14, or 15.
30

44. The polypeptide of Claim 43 which is covalently modified with a water-soluble polymer.

45. The polypeptide of Claim 44 wherein the
35 water-soluble polymer is selected from the group consisting of polyethylene glycol, monomethoxy-

polyethylene glycol, dextran, cellulose, poly-(N-vinyl pyrrolidone) polyethylene glycol, propylene glycol homopolymers, polypropylene oxide/ethylene oxide copolymers, polyoxyethylated polyols, and polyvinyl
5 alcohol.

46. A composition comprising a nucleic acid molecule of Claims 1, 2, or 3 and a pharmaceutically acceptable formulation agent.
10

47. A composition of Claim 46 wherein said nucleic acid molecule is contained in a viral vector.

48. A viral vector comprising a nucleic acid
15 molecule of Claims 1, 2, or 3.

49. A fusion polypeptide comprising the polypeptide of Claims 13, 14, or 15 fused to a heterologous amino acid sequence.
20

50. The fusion polypeptide of Claim 49 wherein the heterologous amino acid sequence is an IgG constant domain or fragment thereof.

51. A method for treating, preventing or ameliorating a medical condition comprising administering to a patient the polypeptide of Claims 13, 14, or 15 or the polypeptide encoded by the nucleic acid of Claims 1, 2, or 3.
25

52. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:
30

(a) determining the presence or amount of
35 expression of the polypeptide of Claims 13, 14, or 15

or the polypeptide encoded by the nucleic acid molecule of Claims 1, 2, or 3 in a sample; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

53. A device, comprising:

(a) a membrane suitable for implantation; and

(b) cells encapsulated within said membrane, wherein said cells secrete a polypeptide of Claims 13, 14, or 15, and wherein said membrane is permeable to said protein and impermeable to materials detrimental to said cells.

54. A method of identifying a compound which binds to a polypeptide comprising:

(a) contacting the polypeptide of Claims 13, 14, or 15 with a compound; and

(b) determining the extent of binding of the polypeptide to the compound.

55. A method of modulating levels of a polypeptide in an animal comprising administering to the animal the nucleic acid molecule of Claims 1, 2, or 3.

56. A transgenic non-human mammal comprising the nucleic acid molecule of Claims 1, 2, or 3.

57. A homodimer of $\beta 10$ polypeptide.

58. A heterodimer of $\beta 10$ polypeptide and another polypeptide.

59. The heterodimer of claim 58 in which the other polypeptide is $\alpha 2$ polypeptide.

5 60. A naturally occurring variant of the $\beta 10$ homodimer of claim 57 or the $\beta 10$ heterodimer of claims 58 or 59.

10 61. A vector comprising nucleic acid molecules encoding $\beta 10$ polypeptide and another polypeptide.

62. The vector of claim 61 in which the other polypeptide is $\alpha 2$.

15 63. A host cell comprising the vector of Claim 61.

20 64. The host cell of Claim 63 that is a prokaryotic cell.

65. The host cell of Claim 63 that is a eukaryotic cell.

25 66. A process of producing a heterodimer of $\beta 10$ and another polypeptide comprising culturing the host cell of Claim 63 under suitable conditions to express the heterodimer, and optionally isolating the heterodimer from the culture.

30 67. The process of claim 66 in which the other polypeptide is $\alpha 2$.

68. A heterodimer produced by the process of Claim 66 or 67.

69. A process for determining whether a compound modulates β 10 heterodimer activity or production comprising exposing a cell according to Claim 63 to the compound, and measuring β 10 heterodimer activity or production in said cell.

70. An antibody produced by immunizing an animal with a β 10 homodimer or β 10 heterodimer.

71. An antibody or fragment thereof that specifically binds the β 10 homodimer of claim 57 or naturally occurring variant thereof.

72. An antibody or fragment thereof that specifically binds the β 10 heterodimer of claim 58 or naturally occurring variant thereof.

73. The antibody of Claims 71 or 72 that is a monoclonal antibody.

74. A hybridoma that produces the monoclonal antibody of claim 73 which is specific to the β 10 homodimer.

75. A hybridoma that produces the monoclonal antibody of claim 73 which is specific to a β 10 heterodimer.

76. A method of detecting or quantitating the amount of β 10 homodimer using the antibody of claim 71.

77. A method of detecting or quantitating the amount of a β 10 heterodimer using the antibody of

claim 72.

78. A selective binding agent or fragment thereof that specifically binds at least one of the following:

5

a) the β 10 homodimer of claim 57;

b) a fragment of the β 10 homodimer of claim 57;

and

c) a naturally occurring variant of (a) or (b).

10

79. The selective binding agent of Claim 78 that is an antibody or fragment thereof.

15

80. The selective binding agent of Claim 78 that is a humanized antibody.

81. The selective binding agent of Claim 78 that is a human antibody or fragment thereof.

20

82. The selective binding agent of Claim 78 that is a polyclonal antibody or fragment thereof.

83. The selective binding agent Claim 78 that is a monoclonal antibody or fragment thereof.

25

84. The selective binding agent of Claim 78 that is a chimeric antibody or fragment thereof.

30

85. The selective binding agent of Claim 78 that is a CDR-grafted antibody or fragment thereof.

86. The selective binding agent of Claim 78 that is an anti-idiotypic antibody or fragment thereof.

87. The selective binding agent of Claim 78 which is a variable region fragment.

88. The variable region fragment of Claim 87
5 which is a Fab or a Fab' fragment.

89. A selective binding agent or fragment thereof comprising at least one complementarity determining region with specificity for a $\beta 10$ homodimer.
10

90. The selective binding agent of Claim 78 which is bound to a detectable label.

91. The selective binding agent of Claim 78 which
15 antagonizes $\beta 10$ homodimer biological activity.

92. A selective binding agent or fragment thereof that specifically binds at least one of the following:

- 20 a) the $\beta 10$ heterodimer of claims 58 or 59;
b) a fragment of the $\beta 10$ heterodimer of claims 58 or 59; and
c) a naturally occurring variant of (a) or (b).

25 93. The selective binding agent of Claim 92 that is an antibody or fragment thereof.

94. The selective binding agent of Claim 92 that is a humanized antibody.
30

95. The selective binding agent of Claim 92 that is a human antibody or fragment thereof.

96. The selective binding agent of Claim 92 that

is a polyclonal antibody or fragment thereof.

97. The selective binding agent of Claim 92 that is a monoclonal antibody or fragment thereof.

5

98. The selective binding agent of Claim 92 that is a chimeric antibody or fragment thereof.

99. The selective binding agent of Claim 92 that is a CDR-grafted antibody or fragment thereof.

10

100. The selective binding agent of Claim 92 that is an anti-idiotypic antibody or fragment thereof.

101. The selective binding agent of Claim 92 which is a variable region fragment.

15

102. The variable region fragment of Claim 101 which is a Fab or a Fab' fragment.

20

103. A selective binding agent or fragment thereof comprising at least one complementarity determining region with specificity for a $\beta 10$ heterodimer.

104. The selective binding agent of Claim 92 which is bound to a detectable label.

25

105. The selective binding agent of Claim 92 which antagonizes $\beta 10$ heterodimer biological activity.

30

106. A method for treating, preventing, or ameliorating a disease, condition, or disorder comprising administering to a patient an effective amount of a homodimer according to claim 57, a heterodimer according to claim 58, or a selective

35

binding agent that specifically binds said homodimer or heterodimer or fragment or naturally occurring variant thereof.

5 107. A composition comprising the homodimer of claim 57, or the heterodimer of claim 58, or a naturally occurring variant of said homodimer or heterodimer, or a fragment of said homodimer or heterodimer, or a selective binding agent of any of the
10 foregoing, and a pharmaceutically acceptable formulation agent.

108. The composition of Claim 107 wherein the pharmaceutically acceptable formulation agent is a
15 carrier, adjuvant, solubilizer, stabilizer, or anti-oxidant.

109. The homodimer of Claim 57 or naturally occurring variant thereof which is covalently modified
20 with a water-soluble polymer.

110. The homodimer of Claim 109 wherein the water-soluble polymer is selected from the group consisting of polyethylene glycol, monomethoxy-polyethylene
25 glycol, dextran, cellulose, poly-(N-vinyl pyrrolidone) polyethylene glycol, propylene glycol homopolymers, polypropylene oxide/ethylene oxide co-polymers, polyoxyethylated polyols, and polyvinyl alcohol.

30 111. A fusion polypeptide comprising the homodimer of Claim 57 or naturally occurring variant thereof which is fused to a heterologous amino acid sequence.

112. The fusion polypeptide of Claim 111 wherein
35 the heterologous amino acid sequence is an IgG constant domain or fragment thereof.

113. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

- 5 (a) determining the presence or amount of expression of the homodimer of Claim 57 or naturally occurring variant thereof; and
- (b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the
- 10 presence or amount of expression of the homodimer.

114. A device, comprising:

- (a) a membrane suitable for implantation; and
- (b) cells encapsulated within said membrane,
- 15 wherein said cells secrete a homodimer of Claim 57 or naturally occurring variant thereof, and wherein said membrane is permeable to said homodimer and impermeable to materials detrimental to said cells.

20 115. A method of identifying a compound which binds to a homodimer comprising:

- (a) contacting the homodimer of Claim 57 or naturally occurring variant thereof with a compound; and
- 25 (b) determining the extent of binding of the homodimer to the compound.

116. A method of modulating levels of a homodimer or heterodimer in an animal comprising administering to

30 the animal the nucleic acid molecule of Claims 1, 2, or 3.

117. A transgenic non-human mammal comprising the nucleic acid molecule of Claims 1, 2, or 3.

118. The heterodimer of Claim 58 or naturally occurring variant thereof which is covalently modified with a water-soluble polymer.

5

119. The heterodimer of Claim 118 wherein the water-soluble polymer is selected from the group consisting of polyethylene glycol, monomethoxy-polyethylene glycol, dextran, cellulose, poly-(N-vinyl pyrrolidone) polyethylene glycol, propylene glycol homopolymers, polypropylene oxide/ethylene oxide co-polymers, polyoxyethylated polyols, and polyvinyl alcohol.

120. A fusion polypeptide comprising the heterodimer of Claim 58 or naturally occurring variant thereof fused to a heterologous amino acid sequence.

121. The fusion polypeptide of Claim 120 wherein the heterologous amino acid sequence is an IgG constant domain or fragment thereof.

122. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

(a) determining the presence or amount of expression of the heterodimer of Claim 58 or naturally occurring variant thereof; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the heterodimer.

123. A device, comprising:

(a) a membrane suitable for implantation; and

(b) cells encapsulated within said membrane,
wherein said cells secrete a heterodimer of Claim 58 or
naturally occurring variant thereof, and wherein said
membrane is permeable to said heterodimer and
5 impermeable to materials detrimental to said cells.

124. A method of identifying a compound which
binds to a heterodimer comprising:

(a) contacting the heterodimer of Claim 58 or
10 naturally occurring variant thereof with a compound;
and

(b) determining the extent of binding of the
heterodimer to the compound.